cesses (appropriately and importantly including both biochemistry and biophysics/biomechanics facets of dynamics). Some other areas at the forefront of cell biology that could fall into this combination of categories are neglected; among these I might suggest protein and nucleic-acid regulatory processes underlying gene expression, ligand/receptor binding and trafficking processes, and protein signal transduction networks. These are all exciting areas that should benefit tremendously from increased devotion of computational modeling efforts. From a wider perspective, many dynamic molecular-level cell processes can be analyzed productively via computational techniques other than differential equations characterizing physico-chemical mechanisms. That is, while differential equations derived from underlying mechanistic hypotheses are wonderfully capable of simulating dynamic processes to generate predictions based on those hypotheses, at least two other outstanding challenges in cell biology that could benefit from computational analysis methods can be posed.

One challenge is the elucidation of hypotheses, in the first place, for operation of a cellular process for experimental systems in which the key molecular components and the topology of their interactions are not well established. An enticing promise of systems biology, in its genomics and proteomics and metabolomics (etc.) mode, is efficient production of experimental data that can be "mined" in an unbiased, "data-driven" manner to glean potential relationships among variables of interest. The types of computational techniques employed for data-mining tasks are typically based on statistical or vector space methods rather than on differential equations, and are not treated in this particular text. The resulting potential relationships, of course, suggest physico-chemical hypotheses for operation of the molecular components represented by the "omics" variables, which can then be transformed into differential equation-based computational models for testing predictions thereof. This hypothesis-formation step is by now the "traditional" domain of bioinformatics, but it is nonetheless a significant area for computational cell biology in facilitating a swift growth in the number of experimental problems that can be addressed by the kind of physico-chemical models articulated in this text at hand.

An additional challenge is how to recover intuitive insights about operation of a cell process of interest, even when successful simulation of the process by a physico-chemical differential equation model has been achieved. Computational prediction of the outcome of the next experiment is essential for building confidence in the validity of the model hypotheses, but does not necessarily simultaneously bring intuitive understanding about why that outcome was obtained. Here again the type of mathematics that can be brought to bear on this question may go beyond what is presented in this text. For instance, Boolean logic, Bayesian network, or Markov chain methods may be gainfully employed to discern how certain variables influence others or how multiple variables combine to influence an outcome.

Thus, as the field of computational cell biology continues to grow, I anticipate further benefit will arise from additional texts that comprise a broader set of cell biology topics and a more comprehensive battery of computational approaches, and address a greater scope of cell biology problems across hypothesis generation, hypothesis testing, and intuition development. But achieving that comfortable marriage will likely require a decade of continuing work by many researchers tackling a variety of particular problems. In the meantime, this current book is certainly the best available for the present early courtship stage, and I will recommend it enthusiastically to all my own students and colleagues.

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Another View of Developmental Biology?

Molecular Principles of Animal Development
By Alfonso Martinez Arias and Alison Stewart
Oxford: Oxford University Press (2002).
350 pp. $42.95

Developmental biology sets out to explain how plants and animals develop. This is a very complex problem and, as such, its solution demands the use of techniques from a variety of disciplines. Hence, developmental biology today is a multidisciplinary endeavor that rests chiefly on four pillars: morphology (embryology), genetics, molecular biology, and cell biology. Its goal is to provide as complete a description of ontogenesis as possible, together with a causal explanation of the mechanisms involved. By applying the techniques and way of thinking of four of the major parcels of biology to the search for a solution of the problem of "development," researchers have achieved what might be considered a synthesis of biological disciplines.

The problem of "development"—where do we come from and how do we come to be—has occupied the human mind certainly since long before the Classical period (see, for example, the discussion on Egyptian and Indian antiquity in Joseph Needham's *A History of Embryology, Second Edition* [New York: Abelard Schuman], 1959); embryological work goes back to the Presocratic period, at least. However, developmental biology as the application of a combination of biological disciplines to the solution of the problem of "development" is a very young science. In the late 1930s, Donald Poulson started investigating embryonic *Drosophila* mutants to show that genes play a role in development (Erwin Baur had collected and analyzed mutants affecting flowering in snapdragons even earlier); and Joseph Needham, Conrad Waddington, Johannes Holtfreter, and others became interested in the chemical nature of Spemann's "Organisator" around the same time. But 30 to 40 more years were to pass before, in the 1970s and 1980s, genetics and molecular biology, followed a little later by cell biology, formed a partnership with embryology in a concerted and systematic attempt to analyze how animals develop. A similar approach was soon adopted to understand plant development. Since the early 1980s, the scientific strategy of dissecting development from several different points of view simultaneously has become firmly established in everyone's mind. Indeed, as I will argue below, the philosophical attitude of developmental biologists has changed, too. Idiosyncrasy determines that some researchers put more emphasis in morphology and others in genetics or molecular biology; but the general orientation of their work, its multidisciplinary character, is common for all.

There are many books on Developmental Biology, some of which are better than others. In accordance with the multidisciplinary, synthesizing character of the discipline, most books try to cover embryological, genetic, and molecular and cell biological aspects of ontogenesis, to provide a complete description of development. Moreover, ontogenesis is treated historically, decomposing it in stages, thus establishing a temporal and spatial framework for reference, following conventions sanctioned by the experience of many years. In such books, students are confronted with stages, like gastrulation or neurulation; with developmental processes, like myogenesis or development of the pancreas; with mechanisms and concepts, like lateral inhibition or induction, positional information, determination or community effect (in most books, though, concepts only make rare appearances!). Model organisms, like *Arabidopsis*, *C. elegans*, sea urchin, *Drosophila*, zebrafish, *Xenopus*, chicken, and mouse, play a prominent role and frequently each one receives particular treatment. An excellent example is Scott F. Gilbert's *Developmental Biology, Sixth Edition* [Sunderland, MA: Sinauer], 2000).

The book reviewed here is somewhat unorthodox, in that it aspires to break with this tradition. In accordance with its title, the book is focused on the molecular and cell biological aspects of development. In the Preface, the authors write "*In this book we explore the idea that developmental biology can be discussed from the point of view of the molecules and the processes that drive the shaping of embryos, rather than from the point of view of the organisms or its constituent parts*." And they indeed attain that goal—at least the one announced in the first part of their sentence. Thus, in chapters 2–5 the reader is presented with the basic tenets of the molecular biology of development, whereas chapters 6 and 7 discuss features of cells and their behaviors relevant for development, like the cell cycle, cell adhesion and cell polarity, cell death, and many more. But they fail to achieve the goal implied in the second part of the sentence.

I agree with the authors that "*...precise descriptions of developing embryos... ...shed little light on the molecular elements involved or the nature of the processes they mediate*"(how could they?). However, I part company with them when they argue that embryology is not needed "*...to answer the important questions*," or when they claim that "*... developmental biology is not embryology*" (I would like to believe that this is a typo, and that the authors want to say that developmental biology is *not only* embryology). One is relieved to read that they "*...do not think that one should dispense with such descriptions altogether. However, they only provide a framework for thinking about molecular interactions...*" In accordance with this conviction, the authors try to discuss development with as few references to the organisms as possible. They fail, because chapters 8–12, which account for 175 of 399 printed pages of text (44%), present several examples of developmental events in particular species. The examples treated include the generation of lineages, the role of morphogens, myogenesis, and neurogenesis in *Drosophila* and in vertebrates, patterning of the vulva in *C. elegans*, the limbs in vertebrates and the wing in *Drosophila*, tooth development, and the development of branched structures—in other words, some of the most interesting and urgent problems in developmental biology. Indeed, molecular and cell biological aspects occupy a prominent place in the discussion of these developmental processes; their embryological aspects are not considered in any great detail. But the authors acknowledge that it is difficult to talk about development without speaking of developing organisms, and try in this manner to justify the substance of the last five chapters of the book, without betraying the cause that they have espoused.

Taking everything into account: in my view this is one of the good books on the discipline. The approach that informs the text, the emphasis on molecules, is not new (witness from Joseph Needham's *Chemical Embryology*, back in 1931; through Eric Davidson's *Gene Activity in Early Development, Third Edition*, 1986; to the chapters on development in Bruce Alberts et al., *Molecular Biology of the Cell, Fourth Edition*, 2002, or in Harvey Lodish et al., *Molecular Cell Biology, Fourth Edition*, 2000; and others). However, this is certainly the first time that an up-to-date, comprehensive treatment of molecular and cell biology focused on animal development has become available. Moreover, although the text of the book is dominated by facts, these facts are embedded in concepts—and this constitutes a most enjoyable and valuable feature of the book. To justify their approach to writing yet another book on development, the authors state that the change in methodology necessitates a change "*...in the way the subject is taught.*" The question of whether teachers of developmental biology should put more emphasis on molecular and cell biological aspects reminds me of discussions, held many years ago, about whether teaching genetics to undergraduates should begin with Mendel or with the structure of the DNA. Hence, I applaud the intentions expressed by the authors of this book, and consider that an emphasis on molecular and cell biology is perfectly adequate for a book on developmental biology in the 21st century. As a textbook for undergraduate students, however, the value of this book is questionable. The level of detail in each chapter is too high, the text too dense, and the style too personal. Much prior knowledge is actually required for the reader to follow the text properly and to appreciate its virtues. The book, however, is excellent for advanced-level graduate students and postgraduates, as a rich source of information and references on developmental concepts. The authors are not to be blamed for two really weak points of the current edition, namely the size of the figures and the typeface. Both are very small and certainly do not contribute to the book's readability. But not only are the letters small; they are also very pale and the text is printed in two columns. Reading this text is by no means an easy exercise. The publisher has failed to match the level of expertise displayed by the authors in writing the text and drawing the figures, both of which deserve much more space and a more professional treatment. This is very regrettable and it should be improved in future editions in interest of a broader audience.

The insistence with which the authors refer to their intention to neglect embryology, to concentrate on molecular and cell biology, is unfortunate. In fact, the authors tacitly contradict their stated intention, as I have tried to show above, and even with the focus on molecules they pay much more attention to developing systems than was apparently intended initially. For obvious reasons, embryology (morphology) is, and will remain, an essential part of developmental biology; untangling ontogenesis will require the continued use of the multidisciplinary approach that has come to fruition during the last 30 years.

In a sense, developmental biology is Systems Biology: developmental biology must use a systems analytical approach in its attempts to cope with the complexity of ontogenesis; the objects it studies ultimately have to be understood from a holistic viewpoint. In the introduction to a special issue of *Science* on Systems Biology published last year (Whole-istic Biology, Science *295*, 1661, 2002), Chong and Ray stated "*...In his* (Ludwig v. Bertalanffy's) *view, old-fashioned science 'tried to explain observable phenomena by reducing them to an interplay of elementary units investigatable independently of each other.' Contemporary science, on the other hand, recognized the importance of "wholeness", defined as 'problems of organization, phenomena not resolvable into local events, dynamic interactions manifest in the difference of behavior of parts when isolated or in higher configuration, etc.; in short, 'systems' of various orders not understandable by investigation of their respective parts in isolation.' "* One can share v. Bertalanffy's opinion (exposed in 1941) or dissent from it. In any case, developmental problems must be tackled in their entire complexity, and this of course requires the detailed and simultaneous consideration of all the component parts of developing systems. The difficulty remains to integrate all data in the wider context, a task for which there is as yet no compelling paradigm.

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